Holoprosencephaly in China: Findings from a Population-based Surveillance System

Cynthia A. Moore, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA, USA. Tel: (770) 488-7163, fax: (770) 488-7197, email: cmoore1@cdc.gov

In the northern provinces of China, the birth prevalence of neural tube defects (NTDs) is among the highest in the world--at about 6 per 1,000 births in rural areas. The Centers for Disease Control and Prevention and Beijing Medical University (now Peking University Health Science Center) collaborated on a folic acid community intervention project from 1993 to 1995 in both the high incidence area in northern China and a lower incidence area in the south where NTD rates are about 1 per 1,000 births. One aspect of the project is a unique, on-going population-based birth defects surveillance program that surveys 150,000 births per year in 2 provinces in the north and 2 provinces in the south. The surveillance system uses photographs to document birth defects and provides baseline rates for NTDs and other external structural birth defects. Although holoprosencephaly was not one of the 26 birth defects originally illustrated in the field atlas for the project, photographs were requested for any infant with external features that were perceived to be abnormal by the local health care workers. These photographs are reviewed by 3 pediatricians and a clinical geneticist and assigned a definitive diagnosis when possible. Since imaging studies are rarely obtained on any infant in the mostly rural surveillance area, the diagnosis of "holoprosencephalic face" was made based on facial features consistent with one of the clinical types of holoprosencephaly.

Thirty-five infants with holoprosencephalic face were identified from 1993 to 1996 in the surveillance area. In both the northern and southern regions, females outnumbered males with a male to female ratio of 0.3:1.The birth prevalence of holoprosencephalic face was twice as high in the northern region; however, when infants with a concomitant NTD were excluded, the rates in two regions equalized at about 0.6 per 10,000 births. Overall, the rates were comparable to those seen in the Metropolitan Atlanta Congenital Defects Program (MACDP) from 1968 to 1982 when ascertainment depended on the recognition of characteristic facial features.

Two nonrandom and specific associations were also found in this population. The first of these associations was holoprosencephalic face with severe ear anomalies. The frequency of anotia or microtia in infants with holoprosencephalic face was 22% (600 times background population rate). This association was confirmed in two other surveillance populations (MACDP and Italian Birth Defects Multicentric Registry) and suggests a common etiology most likely due to abnormal neural crest cell migration. A second nonrandom association was holoprosencephalic face with neural tube defects. The rate of holoprosencephalic face among infants with craniorachischisis or anencephaly was 170 times greater than the general population rate.

The descriptive epidemiology of holoprosencephaly in various populations may provide clues for future etiologic investigations into the genetic and environmental determinants of holoprosencephaly and related malformations.

References:

Rasmussen SA, Moore, CA, Khoury MJ, Cordero JF. Descriptive epidemiology of holoprosencephaly and arhinencephaly in metropolitan Atlanta, 1968-1992. *Am J Med Genet* 66:320-333, 1996.

Berry RJ, Li Z, Erickson D, Li S, Moore CA, et al. Preventing neural-tube defects with folic acid in China. *New Engl J Med*, 341:1509-1517, 1999.